

## RESEARCH ARTICLE

# Epidemiology of Childhood Cancer in Northwest Iran

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### Abstract

This case series study was performed for all 83 children below 14 years old suffering from cancer during 2010-2013 who were registered in Ardabil pediatric cancer registry (APCR). The required data were collected by questionnaire and analyzed with SPSS.19 statistical methods software. Some 51 (61.4%) of cases were male. The mean age of patients was 5.8 years. Of the total, 60 (72.3%) of cases were from urban areas. Results showed that leukemia with 54.2%, CNS with 12% and neuroblastoma with 8.4% were the most prevalent childhood malignancies in Ardabil province. Based on the under 14 year old population estimated from Ardabil province, the cumulative incidence rate was 95.4 patients per one million. The incidence rate was relatively high so that childhood cancers should be considered as an important issue in health policy making in Ardabil province of Iran.

**Keywords:** Childhood - cancer - incidence rate - Iran

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### Introduction

Cancer incidence is the third cause of death in Iran after coronary heart disease and accidents. (Naghavé et al., 2006) However; cancer is a rare disease among children <15 years old. The incidence rate of Childhood cancer is estimated by World Health Organization (WHO) as about 100 per million children. Childhood cancers are rare, representing between 0.5% and 4.6%\* of all cancers. The overall incidence rates of childhood cancer vary between 50 and 200 per million children across the world. (Mehdiabadi et al., 2014), Neoplasms are the second leading cause of death in children < 14. (Kadan-lottick et al., 2007) Childhood cancer rates have been rising slightly for the past few decades. About 1,310 children younger than 14 years old are expected to die from cancer in 2013. (Arora et al., 2007) Epidemiology has a main role in better understanding of cancer causes in children. (Philip et al., 2012) The rate of cancer incidence varies among different communities and races that can be related to Genetic predisposition, early or late exposure to infections and other affecting environmental factors. (Kadan-lottick et al., 2007) Although many genetic conditions are associated with increased risk of childhood cancer, these conditions are supposed to occur only in less than 5% of all cancer cases. (Kaatsch et al., 2006; Mousavi et al., 2010) A literature review on published articles was conducted by using different search showed that the incidence rate of childhood cancer in Iran was 48 to 112 and 51 to 144 per million among girls and boys in

multi geographical settings, respectively. (Mousavi and et al., 2010) Other studies showed various incidence rates of cancer in childhood. Childhood cancer is not a single disease and has various types and pathogenic causes with different histopathology features and occurs in different places of human body. (Stiller et al., 2009; Lacour et al., 2014; Arora et al., 2009) Leukemia (incidence rate =8 to 62/million), central nervous system tumors (CNS) (3 to 22) and Lymphoma (3 to 23) are the prevalent cancers in childhood. (Mousavi et al., 2010) The first step in controlling the burden of cancer is collecting data about frequency, type and places of cancer incidence that can be done by the registered cancer cases in surveillance system. Ardabil cancer registry is a population based cancer registry i.e. active collection of data on all malignant tumors and all CNS tumors (malignant or benign) occurring in a geographically defined population are preserved. In the mid-1999, Ardabil cancer registry started its activities with compilation of data on patients diagnosed as cancer only based on pathologic reports that were gathered from private and community pathology centers. (Amani et al., 2013) The population of Iran is about 78 million where 30% are children and the population covered by the registry area in this study comprises 9 urban districts and their related rural districts, with a total population of 1.3 million. 1.9 % of the total population of Iran is contained within a geographical area of approximately 17953 Square kilometers in northwest of country. Ardabil Province is one of the provinces located in northwestern Iran, an area 70 km inland from the western

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Caspian coastline, with an area of about 17953 km<sup>2</sup> of the total area of Iran (Figures 1 and 2). According to the 2010 census, the population of Ardabil province is 1,284,214 (1.7% of the total population of Iran. (Amani et al., 2013; Naghavi et al., 1999; Farahmand et al., 2011)

In Iran, about 4% of deaths of children < 5 years, 13% children in age group 5-15 years and 15% of children < 15 years loss of life. (Farahmand et al., 2011) According to the importance of childhood cancer and lack of epidemiological study about childhood cancers in Ardabil province, the aim of this study was to assess descriptive epidemiology of childhood cancer in Ardabil province.

**Materials and Methods**

This case-series study has been done on 83 children younger than 14 years old during 2010-13 with cancer that has been pathologically confirmed. There wasn't registered any mortality in study duration. In order to calculate incidence rate, we used Ardabil province population during study years and estimated the cumulative incidence rate and incidence rate for study years. Case definition: Ardabil pediatric cancer registry (APCR) registered only primary cancers while additional tumors that result from the invasion or metastasis of cancer to other organs were not considered. Malignant tumors of all organs were registered based on the International Agency for Research on Cancer (IARC) standards. Ardabil Cancer Registry is only one referral center for registry childhood cancers. All cancer cases aged between 0-14 years at the time of diagnosis (during 2011 to 2013) were enrolled in this study. Data on newly diagnosed (incident) cancer cases were collected from all public and private diagnostic and therapeutic centers (hospitals, pathology/laboratory centers, imaging centers and some of the specialist physician's private offices) of the whole

province. Required data such as sex, age, pathology of cancer, place of residence and etc were collected and included in a checklist form. Collected data analyzed by statistical methods like chi-square test in SPSS.19 software. The significant level was p<0.05.

**Results**

In this study, 83 cancer cases entered during study years. 51 (61.4%) of cases were male and rest of them were female by sex ratio 1.6 to 1. The mean age of patients was 5.8 4.2 and 41% were in age group 1-4 years. 60 (72.3%) of cases were from urban area. Results showed that leukemia with 45 (54.2%), CNS with 12% and Lymphomas with 8.4% were the most prevalent malignancies in Ardabil province (figure 1). Form leukemia cases 86.7% were acute lymphatic leukemia (ALL). The cumulative incidence rate was 95.4 patients per one million. More incidence rate was in year 2011 with 92.8 per 1000000.

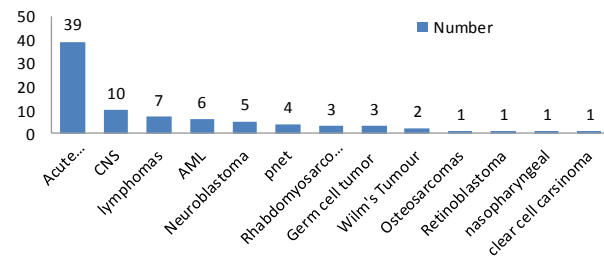
The cumulative incidence rate in all children; girls and boys were 95.4, 85.9 and 10.3 per 1000000 of population. The prevalence of Leukemia and other lesions in male was more than female but there was no significant difference between sex and type of malignancy (Table.1). There were no differences in pattern of cancer between years and place of residence which have similar pattern.

ALL with 47% were the prevalent cancer pathology in all age groups and also, most of ALL cases were in age groups 1-4 with 41% (Table.2).

The ASR in age groups 0-4 and 5-9 in male was more than female and in urban population the ASR in age groups 5-9 and 10-14 was more than rural population (Table 3).

**Table 1. Distribution of Malignant Lesions by Sex in Cases**

	Others(%)N	Leukemia(%)N
Male	(71.1)27	(53.3) 24
Female	(28.9) 11	(46.7) 21



**Figure 1. Frequency of Malignant Lesions in Cases**

**Table 2. frequency Distribution of Malignant Lesions by Age in Cases**

Type	number	<1(%)	1-4(%)	5-9(%)	10-14(%)	Crude rate
ALL	39	5.1	41	35.9	17.9	4.48
CNS	10	20	50	0	30	1.15
AML	6	16.7	33.3	33.3	16.7	0.69
Neuroblastoma	5	20	60	0	20	
Pent	4	0	0	50	50	
Lymphomas	7	0	14.3	57.1	28.6	
Rhabdomyosarcomas	3	0	66.7	33.3	0	
Germ Cell Tumor	3	33.3	66.7	0	0	
Wilm's Tumour	2	0	100	0	0	
Osteosarcomas	1	0	0	0	100	
Retinoblastoma	1	0	0	100	0	
Nasopharyngeal	1	0	0	0	100	
Clear Cell Carcinoma	1	0	100	0	0	
Total	83	8.4	41	28.9	21.7	

**Table 3. Total Incidence and Age Standard Rate by Sex and Residence Place**

Rural		Urban		Female		Male		Age groups
ASR	N	ASR	N	ASR	N	ASR*	N	
47.5	15	46.9	26	37.6	14	54.3	27	0-4
15.8	5	34.3	19	24.2	9	30.2	15	5--9
9.4	3	27.1	15	24.2	9	18.1	9	10--14

The result of statistical tests by Chi-Square showed that there was a significant differences in ASR between age groups by residence place ( $p=0.011$ ). Also, there was not a significant difference in ASR between age groups by sex of patients which ASR was similar in both sexes.

## Discussion

According to the result of this study, most prevalent cancers in children under 14 years in Ardabil province were: Leukemia (54.2%), CNS (12.1%) and lymphomas with 8.4%, respectively that this result was similar to other study results. [14-15] In this study, most cancers were seen in males with 61.5% which were similar to other studies. (Roshandel et al., 2012; Moradi et al., 2010) Most of cases were in age group 0-4 years. Also, in previous studies in Iran, most of cases were in age group 6-7 years. (Frahmand et al., 2011; Moradi et al., 2010) In Another studies, higher frequency of cancer cases were seen in age group 1-4 years which were similar to our study results. (Jefroudi et al., 2008; Stefan et al., 2015) In Farahmand and et al study, the rate of cancer incidence in males was more prevalent than females and the mean age of cases was 10.3 (SD=2) and the most and least incidence rates were in years 2006 and 2001 with 235 and 64 per 1000000, respectively which was similar to our study results and pattern of cancer in developed countries. (Frahmand et al., 2011). The cancer incidence rate in Iran in boys varied between 48 to 112 and in girls between 51 to 144 per 1000000 in various areas and most prevalent cancers in children under 14 years were Leukemia with incidence rate of 8 to 62, lymphomas with incidence rate of 3 to 23 and CNS with incidence rate of 3 to 22 per 1000000. (Mousavi et al., 2010). The first three childhood cancers in our study were leukemia, CNS tumors and Neuroblastoma; respectively. In United States, in 1995 the most common cancers in children were acute leukemia, CNS tumors, and lymphomas. [21] A study in Mexican republic reported that in some tumors there were more cases in female (retinoblastoma, germ cells tumors) and the principal groups of neoplasm were leukemia, CNS tumors, and lymphomas and the combined frequency for these three groups was 62.6% to 77.2%. (Gutierrez et al., 2007). In German Childhood Cancer Registry (GCCR) during 1980-2005 the three top cancers were leukemia, Hodgkin's disease and Non Hodgkin lymphoma. Also age, sex and period of diagnosis showed no influence on the distribution of diagnoses. (Spallek et al., 2008). The results of Golestan study during 2004-2006 showed that leukemia, CNS tumors and lymphomas were first three childhood cancers. As mentioned above, the present results showed some differences with the results of other studies. This may be due to the specific conditions in Ardabil

province resulting in higher incidence of Neuroblastoma in comparison with Lymphomas. Another explanation for this difference is under-reporting of Lymphoma tumors because of diagnostic difficulties. Further studies are needed to determine the actual reasons of the above mentioned differences. The incidence rate of Leukemia and CNS tumors were not the same in females and males. According to the present findings, in Ardabil province, ASRs of leukemia were 51.8 per million in total pediatric population, 48.3 in males and 56.4 in females, during 2010-2013. In another study in Mexican republic during 1998-2000 the ASR of leukemia was 55.4, 58.2 and 49.9 per million in total pediatric populations, males and females, respectively. (Gutierrez et al., 2007) These results were close to the results of Ardabil province. In the present study, CNS tumors were the second common cancer diagnosed in both genders. According to SEER reports the ASR of CNS tumors in the USA during 2004-2007 (27.4/1000000) was considerably higher than ours (11.5 per million) and also, the Golestan study (9.5 per million) lower than our study results. As mentioned above, this may be due to the specific conditions of Ardabil or Golestan province or as a result of under-reporting of these tumors. The third common cancer type was Neuroblastoma in Ardabil Province followed by CNS tumor types. This was different in other regions. (Moradi et al., 2010; Jefroudi et al., 2008) But in other parts leukemia is followed by CNS tumors. It means that lymphomas ranked as the third common cancer type and the second one was CNS tumors.

Leukemia was the most common childhood cancer in Ardabil province of Iran. CNS tumors and Neuroblastoma were the second and third ones, respectively. The incidence rate of these cancers was relatively high in Ardabil province. So, childhood cancers should be mentioned as an important issue in health policy making in Ardabil province of Iran.

Finally, a study about correlation between the risk of cancer suffering and survival of cancer cases was recommended for future studies. Because of some cancer cases may be not registered or non-referred during study years for APCR, so the real estimation Cumulative and incidence rate can be influenced by them. It is essential that the effect of geographical differences on childhood cancer incidence rates to be investigated in future studies.

The risk factors for childhood cancer are still unexplained. However, studies had speculated that some factors may have a role on the etiology (ie, specific environmental exposures, ABO blood groups, and Epstein-Barr virus infection). Therefore, more studies and investigation in future would be essential. Considering the population pyramid in Iran shows that the children population decreased from 44% in 1976 to 29% in 2010. The trend of childhood cancer was still unknown up to date as a contemporary backbone for any cancer control program among the nation of Iran.

The data from this study may be used as the baseline information to establish a population-based registry of childhood cancers in the country for health care and research purposes. However, more investigations are needed to develop effective strategies to control these disorders in high risk areas.

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